REMARKS

In view of the amendments and remarks that follow, Applicants respectfully submit that the application is in condition for allowance. Accordingly, applicants request reconsideration of the application, withdrawal of the rejections of record and issuance of a Notice of Allowance.

Claims 1-20 are pending in the application, all of which stand rejected for the reasons of record. Claims 16-20 have been canceled and claims 1 and 7-15 have been amended to put them in better condition for allowance. The amendments are not considered to involve the addition of new matter and entry thereof is respectfully requested.

It is noted and acknowledged that the references cited in the Information Disclosure Statements filed on 10/22/2003 and 12/18/2003 have been made of record.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-5 and 7-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, in Claim 1, the Office considers the recitation of "its enantiomers, diastereomers, pharmaceutically acceptable salts prodrugs or solvates thereof" to be indefinite because it is not clear whether the claim is a compound or composition claim. The Office notes that the Markush recitation should be in alternate form and in singular

Applicants respectfully suggest that the Office read the claim closely as it is already in proper Markush format as shown in the Amendments to the Claims section above.

In Claim 1, the Office notes that the recitation of the term "prodrug" is deemed as indefinite. While disagreeing that the word "prodrug" is indefinite, Claim 1 has been amended to delete the term "prodrug" in order to expedite the prosecution of the claims.

Claim 1 is also considered indefinite because it is not clear what R^{41} is when Z is N. Applicants have reviewed the application and note that this substituent is exemplified as hydrogen and lower alkyl. The claim has been amended to add this definition for R^{41}. This amendment is supported by the disclosure in Examples 24-37.

In Claims 7-10, 12-15 and 20, the Office notes that the recitation of "at least one of the compounds of " renders these claims indefinite. The Office suggests the replacement of this with "one or more". While disagreeing that "at least one" renders the claims indefinite, the claims have been amended to recite "one or more" in order to expedite the prosecution of these claims.

The Office notes that the limitation in Claim 11 "said anti-cancer or cytotoxic agent" has no antecedent basis in Claim 7 (the Claim which it depends therefrom). Claim 11 has been amended to properly depend on Claim 9 which contains the proper antecedent basis.

The Office notes that the recitation of the phrase "including" in claim 11 renders the claim indefinite. Claim 11 has been amended to remove the term "including" in order to put this claim in condition for allowance.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-5 and 7-20 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The Office has summarized the factors to be considered in making an enablement rejection and concluded that the claims are not enabled.

Applicants disagree that the specification does not provide any direction. As noted by the Office, the specification provides more than enough direction to one of ordinary skill in this particular art to prepare prodrugs of the compounds of the invention. References are provided showing various forms of prodrugs and their synthesis. Clearly one skilled in the art would be able to use these references and the knowledge in the art to prepare prodrugs of the instantly claimed compounds.

However, while disagreeing with the Office's conclusion, Claim 1 has been amended to delete the term "prodrug" in order to expedite the prosecution of that Claim and those depending thereon. It is respectfully noted that Claims 8 and 10 depend on Claim 6 which is an independent claim and not subject to the above rejection.

Claims 1-5 and 7-20 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making salts of the claimed

compounds, does not reasonably provide enablement for making solvates of the claimed compounds.

Applicants disagree that the specification does not provide any direction. Clearly one skilled in the art would be able to use the knowledge in the art to prepare solvates of the instantly claimed compounds.

However, while disagreeing with the Office's conclusion, Claim 1 has been amended to delete the term "solvate" in order to expedite the prosecution of that Claim and those depending thereon. It is respectfully noted that Claims 8 and 10 depend on Claim 6 which is an independent claim and not subject to the above rejection.

Claims 16-20 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for treating angiogenesis, does not reasonably provide enablement for treating any proliferative disease, cancer, inflammation, autoimmune disease or "diseases associated with signal transduction pathways operating through growth factor receptors". The Office argues that "the specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The Office goes on to conclude, after considering a number of factors, that undue experimentation would be required to practice Applicants' invention.

While disagreeing with the Office's conclusion, Claims 16-20, as noted above, have been canceled in order to expedite the prosecution of the remaining claims.

Rejections Under 35 U.S.C. § 102

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunt et al. WO 00/71129. The Office notes that Hunt teaches structurally similar pyrrolotriazine compounds It is noted that in the formula (I) on page 3, all variable groups overlap with those of the instant claims

Applicants respectfully traverse the rejection and present the following comments. The compounds disclosed in Hunt et al. differ from the instant compounds in that the instant compounds contain a distinctive pyrrolo-pyridinyl group off of the 6-membered ring of the pyrrolotriazine core. While Hunt may generically disclose this group, none of the over 200 compounds exemplified in Hunt contains this group. Clearly the compounds

disclosed in the instant application would not be considered anticipated by Hunt. Applicants respectfully submit that this ground of rejection should be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-26 (20) (sic) are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunt et al., WO 00/71129. The Office notes that Hunt et al. teaches structurally similar pyrrolotriazine compounds and notes that in the formula (I) on page 3, all variable groups overlap with those of the instant claims. The Office also notes that Example 120 is close to the instant R^{42} and that the point of attachment of such a group is either through the five or six membered ring. The Office also notes that compounds when Z=N or NH or when Z is absent are exemplified.

The Office concludes that it would have been obvious to one having ordinary skill in the art at the time of the invention was made (sic) to make pyrrolotriazine compounds variously substituted with the variables noted as permitted by the reference and expect resulting compounds (i.e., the instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants respectfully traverse the rejection and provide the following comments. It would not be obvious, in view of the differences between the instant compounds and those disclosed in Hunt, to make the instant compounds. The instantly claimed compounds are patentably distinct as noted above. The Office notes that Hunt teaches a number of compounds where Z is absent. However, the instant invention does not claim that Z is absent and requires some sort of linking group between the pyrrolotriazine core and the side group. None of the previously disclosed compounds contain the R^{41} substituent, which is narrowly defined. Applicants submit that Claim 1, as amended, is not anticipated by Hunt et al. and request that this ground of rejection be withdrawn.

Provisional Double Patenting Rejections

Claims 1-5 and 7-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-7, 12 and 16 of co-pending Application No. 09/573,829.

Claims 1-5 and 7-20 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 16-25 of co-pending Application No. 10/441,848.

Finally, Claims 1-5 and 7-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 and 4-19 of co-pending Application No.10/633,997.

While disagreeing with the provisional rejections, Applicants will consider the propriety of filing a Terminal Disclaimer upon notification of allowable subject matter.

In view of the foregoing, Applicants submit that the application, as amended, is in condition for allowance and courteously solicit a Notice of Allowance.

If any fee due is not accounted for herein, please charge such fee to Deposit Account No. 19-3880. If any extension of time is required and not petitioned for, such extension is hereby petitioned for, and it is requested that any fee due in connection therewith be charged to the aforementioned Deposit Account.

The foregoing response is believed to be fully responsive to the outstanding Office Action. If a direct personal communication would advance the prosecution of this application, please contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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